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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/038,730	01/02/2002	Robert M. Abrams	99-0137 (US02)	3733
41696 7590 02/07/2007 VISTA IP LAW GROUP LLP 12930 Saratoga Avenue Suite D-2 Saratoga, CA 95070			EXAMINER SCHNIZER, RICHARD A	
			ART UNIT	PAPER NUMBER
			1635	
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		02/07/2007	PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary

Application No.

10/038,730

Applicant(s)

ABRAMS ET AL.

Examiner

Richard Schnizer, Ph. D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 December 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 32-41, 43, 44, 46, 53-57 and 59 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 32-41, 43, 44, 46, 53-57 and 59 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

An amendment was received and entered on 12/13/06.

Claims 32-41, 43, 44, 46, 53-57, and 59 remain pending and are under consideration in this Office Action.

This Action is NON-FINAL due to new grounds of rejection under 35 USC § 103 not necessitated by Applicant's amendment.

Drawings

No drawings were filed with the application.

Claim Objections

Applicant's amendments overcame the objections to claims 41, 44, and 55 in the previous Action.

Claim 55 is objected to because the penultimate word 'Is' should not be capitalized.

Compliance with Sequence Rules

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the following reason(s). Applicant's attention is directed to the final rule making notice published at 55 FR 18230 (May 1, 1990), and 1114 OG

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29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998). **The specification at page 8, line 2, discloses an amino acid sequence in excess of 3 amino acids that is not accompanied by a SEQ ID NO. Claim 41 discloses the same peptide.** The Application contains no Sequence Listing in either computer readable form or paper form. Applicant must provide:

An initial computer readable form (CRF) copy of the "Sequence Listing".

An initial paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

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For questions regarding compliance to these requirements, please contact:

- For Rules Interpretation, call (571) 272-0951
- For Patentin Software Program Help, call Patent EBC at 1-866-217-9197 or directly at 703-305-3028 / 703-308-6845 between the hours of 6 a.m. and 12 midnight, Monday through Friday, EST.
- Send e-mail correspondence for Patentin Software Program Help @ ebc@uspto.gov.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

Claims 32-41, 43, 44, 46, 53-57, and 59 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Independent claim 32 has been amended to require a “polymeric occlusion mass” with “a molecular weight (MW_w) of at least 10,000 and less than about 500,000”. The specification as filed, while providing support for a polymeric occlusion mass comprising polymers with an average molecular weight of at least 10,000 and less than about 500,000, provides no support for a polymeric occlusion mass with an average molecular weight of at least 10,000 and less than about 500,000. So, the amendment adds new matter to the claims. This rejection can be overcome by amending claim 32 to require that the MW_w of the polymer comprised by the occlusion mass is at least 10,000 and less than about 500,000, if the specification as filed supports such an amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 32-39, 44, 53-55, and 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Evans (US Patent 5,702,361) in view of Greff et al (US Patent 6,015,541).

Evans taught kits, systems, and methods for forming embolisms in blood vessels, e.g. for the treatment of tumors. A mechanical occlusive device such as a metal coil is introduced into a vascular site (e.g., an aneurysm cavity) in conjunction with an embolizing composition comprising a biocompatible polymer and a biocompatible solvent. The biocompatible solvent is miscible or soluble in blood and also solubilizes the polymer during delivery. The biocompatible polymer is selected to be soluble in the biocompatible solvent but insoluble in blood. Upon contact with the blood, the biocompatible solvent dissipates from the embolic composition whereupon the biocompatible polymer precipitates. Precipitation of the polymer in the presence of the non-particulate agent permits the agent to act as a structural lattice for the growing polymer precipitate. In another embodiment, the biocompatible polymer composition can be replaced with a biocompatible prepolymer composition containing a biocompatible prepolymer. See abstract, and column 10, lines 23-28.

Preferred biocompatible polymers include cellulose diacetate and ethylene vinyl alcohol copolymer. In a preferred embodiment, the average molecular weight, as determined by gel permeation chromatography, of the cellulose diacetate composition is from about 25,000 to about 100,000 more preferably from about 50,000 to about 75,000 and still more preferably from about 58,000 to 64,000. See column 5, lines 40-48. Preferably, the polymer composition will comprise from about 2.5 to about 8.0 weight percent of the biocompatible polymer composition based on the total weight of the polymer composition. See column 7, lines 10-18. The particular biocompatible polymer employed is not critical and is selected relative to the viscosity of the resulting polymer solution, the solubility of the biocompatible polymer in the biocompatible solvent, the compatibility of the polymer composition with the non-particulate agent and the like. Such factors are well within the skill of the art. See column 5, lines 34-39. The biocompatible solvent can be a mixture of ethanol and water. See column 6, lines 41-51. In the methods of Evans, the mechanical occlusive device is introduced into the target site prior to the polymer composition by the same or a different catheter. See column 8, lines 13-23, and column 10, lines 11-16.

Although Evans taught the inclusion of a contrast agent in the polymer solution, Evans did not teach a system comprising a bioactive agent in the polymer solution (other than the embolizing polymer). Also, Evans did not teach a polyester polymer.

Greff taught a method of treating tumors by injecting into a blood vessel a composition comprising a radioactive isotope and a polymer dissolved in a biocompatible solvent, wherein the polymer is insoluble in blood. Upon contact with

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blood, the polymer forms an embolism comprising the isotope. The isotope is toxic to the rapidly replicating tumor cells. The composition is delivered via catheter to a blood vessel in the tumor. See abstract and e.g. column 3, lines 32-62. Polymers for use polylactides, polyglycolides, polycaprolactones, polyanhydrides, polyamides, polyurethanes, polyesteramides, polyorthoesters, polydioxanones, polyacetals, polyketals, polycarbonates, polyorthocarbonates, polyphosphazenes, polyhydroxybutyrates, polyhydroxyvalerates, polyalkylene oxalates, polyalkylene succinates, poly(malic acid), poly(amino acids), polyvinylpyrrolidone, polyethylene glycol, polyhydroxycellulose, chitin, chitosan, and copolymers, terpolymers and combinations thereof, as well as gelatin and collagen. See column 5, lines 42-55.

It would have been obvious to one of ordinary skill in the art at the time of the invention to improve the tumor treatment method of Evans by including in the polymer solution a radioactive isotope, as taught by Greff. One would have been motivated to do so in order to gain the advantage of tumor toxicity conveyed by the radioactive isotope. It would have been similarly obvious to use any of the polymers or copolymers set forth in Greff because it is clear that these are art recognized equivalents of the polymers of Evans inasmuch as they are delivered in a pharmaceutically acceptable solution and precipitate after contacting blood. Thus the invention as a whole was *prima facie* obvious.

Claims 40, 41, 43, and 46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Evans (US Patent 5,702,361) and Greff et al (US Patent 6015541) as

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applied to claims 32-39, 44, 53-55, and 59 above, and further in view of Murayama et al (US Patent 5,891,192).

The teachings of Evans and Greff are summarized above and render obvious systems for forming embolisms in blood vessels by using a catheter to deposit at a target site a mechanical occlusive device and a composition comprising a dissolved, blood-insoluble polymer and a bioactive agent, which subsequently forms an embolism together with the mechanical occlusive device at the target site.

Evans also taught that migration of artificial emboli away from a target site, due to poor anchoring of the emboli, was a problem recognized in the art. See column 3, lines 15-34.

Greff also taught that proteins such as collagen could be used as polymers in embolism forming solution, and that mixtures of different polymers could be utilized as well. See column 5, lines 42-55.

These references did not teach the use of fibronectin.

Murayama taught that it was routine in the art to coat mechanical occlusive devices with cell adhesion proteins such as collagen, fibronectin, vitronectin, laminin or fibrinogen. See e.g. abstract, column 1, lines 30-34, and paragraph bridging columns 2 and 3. Such coating increases thrombogenicity and cell adhesion. See e.g. column 3, lines 20-27.

It would have been obvious to one of ordinary skill in the art at the time of the invention to add a cell adhesion protein, such as fibronectin, to the composition of Evans as modified by Greff. Greff envisioned the use of mixtures of different polymers,

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as well as the use of collagen, so inclusion of a cell adhesion protein such as collagen is obvious in view of the teachings of Evans and Greff. Also, Evans recognized that migration of emboli away from target sites due to poor anchoring was a problem, and Murayama taught that coating occlusive devices with cell adhesion proteins such as collagen and fibronectin, was a means of addressing this problem. In view of the teachings of the prior art as a whole, it would have been obvious to substitute fibronectin, or any other cell adhesion protein, for collagen in the composition of Evans as modified by Greff. One would have been motivated to add collagen to the polymers of Evans because Greff taught that collagen was useful for forming embolisms and suggested using mixtures of polymers, and because Murayama taught that the use of cell adhesion proteins in embolism forming compositions improved cell adhesion and thrombogenicity. It would have been obvious to substitute fibronectin for collagen, because Murayama taught that these two proteins were exchangeable equivalents for improving cell adhesion and thrombogenicity. See MPEP 2144.06. Thus the invention as a whole was prima facie obvious.

Claims 56 and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Evans (US Patent 5,702,361) and Greff et al (US Patent 6015541) as applied to claims 32-39, 44, 53-55, and 59 above, and further in view of Park (US Patent 5,925,683).

The teachings of Evans and Greff are summarized above and render obvious methods for forming embolisms in blood vessels by using a catheter to deposit first a

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mechanical occlusive device, and then a composition comprising a dissolved, blood-insoluble polymer and a bioactive agent, which subsequently forms an embolism together with the mechanical occlusive device. The same or different catheters may be used.

The references did not teach a plug of barrier solvent.

Park taught methods of forming embolisms in blood vessels by catheter-mediated delivery of solutions of dissolved, blood-insoluble polymers that form an embolism when contacted by blood. Park taught that when a blood vessel is catheterized, blood often refluxes into the distal end of catheter. Since the polymer of the composition precipitates as the solvent mixes with blood, a polymer solution injected through a catheter could precipitate in the catheter. In such an event, the inventive polymer solution likely would not reach the treatment site. Thus, it is highly desirable to separate the inventive polymer solution from the blood during the period of its delivery through the catheter. A plug of a barrier solvent is suitable for such separation. A 20-30% aqueous ethanol solution is effective as a barrier. See paragraph bridging columns 5 and 6.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use a barrier plug of solvent in the method of Evans as modified by Greff. One would have been motivated to do so because Park taught that premature precipitation of a blood insoluble polymer could result in a failure of the polymer solution to reach the treatment site. This problem is mitigated through the use of a barrier plug. Thus the invention as a whole was prima facie obvious.

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Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, J. Douglas Schultz, can be reached at (571) 272-0763. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Richard Schnizer, Ph.D.
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Art Unit 1635